What is Claimed is:

1. A compound of Formula (I):

$$R_1$$
 A
 E
 E
 R_2
 R_3
 R_4
 R_2

Formula (I)

wherein

A and E are independently selected from the group consisting of a hydrogen substituted

carbon atom and a nitrogen atom; wherein N is independently selected from the group consisting of 1*H*-indole, 1*H*-pyrrolo[2,3-*b*]pyridine, 1*H*-pyrazolo[3,4-*b*]pyridine and 1*H*-indazole;

Z is selected from O or dihydro; wherein when Z is dihydro, each hydrogen atom is attached by a single bond;

10 R₄ and R₅ are independently selected from C₁₋₈alkyl, C₂₋₈alkenyl and C₂₋₈alkynyl, wherein R₄ and R₅ are optionally substituted with oxo;

R₂ is selected from the group consisting of -C₁₋₈alkyl-, -C₂₋₈alkenyl-, -C₂₋₈alkynyl-,
-O-(C₁₋₈)alkyl-O-, -O-(C₂₋₈)alkenyl-O-, -O-(C₂₋₈)alkynyl-O-,
-C(O)-(C₁₋₈)alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl
linking groups are straight carbon chains optionally substituted with one to four
substituents independently selected from the group consisting of C₁₋₈alkyl,
C₁₋₈alkoxy, C₁₋₈alkoxy(C₁₋₈)alkyl, carboxyl, carboxyl(C₁₋₈)alkyl,
-C(O)O-(C₁₋₈)alkyl, -C₁₋₈alkyl-C(O)O-(C₁₋₈)alkyl, amino (substituted with a
substituent independently selected from the group consisting of hydrogen and

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 C_{1-4} alkyl), amino (C_{1-8}) alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), halogen, $(halo)_{1-3}(C_{1-8})$ alkyl, $(halo)_{1-3}(C_{1-8})$ alkoxy, hydroxy, hydroxy (C_{1-8}) alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C₁₋₈)alkyl, $aryl(C_{1-8})alkyl$, heteroaryl $(C_{1-8})alkyl$, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of $C_{1.8}$ alkyl, $C_{1.8}$ alkoxy, $C_{1.8}$ alkoxy($C_{1.8}$)alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and $C_{1.4}$ alkyl), amino $(C_{1.8})$ alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, $(halo)_{1-3}(C_{1-8})$ alkoxy, hydroxy and hydroxy (C_{1-8}) alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl, heterocyclyl, aryl, heteroaryl (wherein cycloalkyl, heterocyclyl, aryl and heteroaryl are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and $C_{1.4}$ alkyl), amino $(C_{1.8})$ alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, (halo)₁₋₃(C₁₋₈)alkoxy, hydroxy and hydroxy(C₁₋₈)alkyl; and, wherein heterocyclyl is optionally substituted with oxo), -(O-(CH₂)₁₋₆)₀₋₅-O-, -O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-O-, -O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-O-, -(O-(CH₂)₁₋₆)₀₋₅-NR₆-, -O-(CH₂)₁₋₆-NR₆-(CH₂)₁₋₆-O-, -O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-NR₆-, -(O-(CH₂)₁₋₆)₀₋₅-S-, -O-(CH₂)₁₋₆-S-(CH₂)₁₋₆-O-, -O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-S-, -NR₆-, -NR₆-NR₇-, $-NR_{6}$ - $(CH_{2})_{1-6}$ - NR_{7} -, $-NR_{6}$ - $(CH_{2})_{1-6}$ - NR_{7} - $(CH_{2})_{1-6}$ - NR_{8} -, $-NR_{6}$ -C(O)-, -C(O)- NR_{6} -, $-C(O)-(CH_2)_{0-6}-NR_6-(CH_2)_{0-6}-C(O) -NR_6-(CH_2)_{0-6}-C(O)-(CH_2)_{1-6}-C(O)-(CH_2)_{0-6}-NR_{7-}$, $-NR_6-C(O)-NR_{7-}$ $-NR_6-C(NR_7)-NR_8-$, $-O-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-S-$, $-S-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-O-$, $-S-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-S-$, $-NR_6-(CH_2)_{1-6}-S-(CH_2)_{1-6}-NR_7-$ and $-SO_2-$ (wherein

 R_6 , R_7 and R_8 are independently selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl(C_{1-8})alkyl, amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), hydroxy(C_{1-8})alkyl, heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl and heteroaryl(C_{1-8})alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, (halo)₁₋₃(C_{1-8})alkoxy, hydroxy and hydroxy(C_{1-8})alkyl; and, wherein heterocyclyl is optionally substituted with oxo));

with the proviso that, if A and E are selected from a hydrogen substituted carbon atom, then R_2 is selected from the group consisting of $-C_{2-8}$ alkynyl-, $-O-(C_{1-8})$ alkyl-O-, $-O-(C_{2-8})$ alkenyl-O-, $-O-(C_{2-8})$ alkynyl-O-, $-C(O)-(C_{1-8})$ alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are straight carbon chains optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, $-C(O)O-(C_{1-8})$ alkyl, $-C_{1-8}$ alkyl-C(O)O-($-C_{1-8}$)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and $-C_{1-4}$ alkyl), amino($-C_{1-8}$)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and $-C_{1-4}$ alkyl), halogen, (halo) $-C_{1-8}$ alkyl, (halo) $-C_{1-8}$ alkoxy, hydroxy,

hydroxy(C_{1-8})alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl, heteroaryl(C_{1-8})alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and

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 C_{1-4} alkyl), amino (C_{1-8}) alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), halogen, $(halo)_{1-3}(C_{1-8})$ alkyl, $(halo)_{1-3}(C_{1-8})$ alkoxy, hydroxy and hydroxy (C_{1-8}) alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl (wherein cycloalkyl is optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, (halo)₁₋₃(C_{1-8})alkoxy, hydroxy and hydroxy(C_{1-8})alkyl), -(O-(CH_2)₁₋₆)₁₋₅-O-, -O-(CH_2)₁₋₆-O-(CH_2)₁₋₆-O-, $-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-O-$, $-(O-(CH_2)_{1-6})_{1-5}-NR_{6-}$, $-O-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-O-, -O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-NR_6-, -(O-(CH_2)_{1-6})_{0-5}-S-,$ $-O-(CH_2)_{1-6}-S-(CH_2)_{1-6}-O-, -O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-S-, -NR_6-NR_{7-},$ $-NR_{6}-(CH_{2})_{1-6}-NR_{7}-$, $-NR_{6}-(CH_{2})_{1-6}-NR_{7}-$ (CH₂)₁₋₆-NR₈-, $-NR_{9}-$ C(O)-, -C(O)-NR₉-, $-C(O)-(CH_2)_{0-6}-NR_6-(CH_2)_{0-6}-C(O) -NR_{6}-(CH_{2})_{0-6}-C(O)-(CH_{2})_{1-6}-C(O)-(CH_{2})_{0-6}-NR_{7}-$, $-NR_{6}-C(O)-NR_{7}-$, $-NR_6-C(NR_7)-NR_8-$, $-O-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-S-$, $-S-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-O-$, -S- $(CH_2)_{1-6}$ -NR₆- $(CH_2)_{1-6}$ -S- and -NR₆- $(CH_2)_{1-6}$ -S- $(CH_2)_{1-6}$ -NR₇- (wherein R₆, R₇ and R₈ are independently selected from the group consisting of hydrogen, C₁₋₈alkyl, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl(C_{1-8})alkyl, amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), hydroxy(C_{1-8})alkyl, heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl and heteroaryl($C_{1.8}$)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino (C_{1-8}) alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), halogen, (halo)₁₋₃(C₁₋₈)alkyl, $(halo)_{1-3}(C_{1-8})$ alkoxy, hydroxy and hydroxy (C_{1-8}) alkyl; and, wherein heterocyclyl is optionally substituted with oxo); and, wherein R₉ is selected from the group

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consisting of C_{1-8} alkyl, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl(C_{1-8})alkyl, amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), hydroxy(C_{1-8})alkyl, heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl and heteroaryl(C_{1-8})alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo) $_{1-3}$ (C_{1-8})alkyl, (halo) $_{1-3}$ (C_{1-8})alkoxy, hydroxy and hydroxy(C_{1-8})alkyl; and, wherein heterocyclyl is optionally substituted with oxo)); and,

R₁ and R₃ are independently selected from the group consisting of hydrogen, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl (wherein alkyl, alkenyl and alkynyl are optionally substituted with a substituent selected from the group consisting of C₁₋₈alkoxy, alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), $(halo)_{1-3}$, $(halo)_{1-3}(C_{1-8})$ alkyl, $(halo)_{1-3}(C_{1-8})$ alkoxy, hydroxy, hydroxy (C_{1-8}) alkyl and oxo), C₁₋₈alkoxy, C₁₋₈alkoxycarbonyl, (halo)₁₋₃(C₁₋₈)alkoxy, C₁₋₈alkylthio, aryl, heteroaryl (wherein aryl and heteroaryl are optionally substituted with a substituent selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino (C_{1-8}) alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, $(halo)_{1-3}(C_{1-8})$ alkoxy, hydroxy and hydroxy (C_{1-8}) alkyl), amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), cyano, halogen, hydroxy and nitro;

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and pharmaceutically acceptable salts thereof.

- 2. The compound of claim 1 wherein R_4 and R_5 are independently selected from C_{1-6} alkyl, C_{2-6} alkenyl and C_{2-6} alkynyl optionally substituted with oxo.
- The compound of claim 1 wherein R₄ and R₅ are independently selected from
 C₁₋₆alkyl, C₂₋₆alkenyl and C₂₋₆alkynyl.
 - 4. The compound of claim 1 wherein R_4 and R_5 are independently selected from C_{1-6} alkyl.
 - 5. The compound of claim 1 wherein R₂ is selected from the group consisting of -C₁₋₈alkyl-, -C₂₋₄alkenyl-, -C₂₋₄alkynyl-, -O-(C₁₋₄)alkyl-O-, -O-(C₂₋₄)alkenyl-O-, -O-(C₂₋₄)alkynyl-O-, -C(O)-(C₁₋₄)alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are straight carbon chains optionally substituted with one to four substituents independently selected from the group consisting of C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkoxy(C₁₋₄)alkyl, carboxyl, carboxyl(C_{1-4})alkyl, -C(O)O-(C_{1-4})alkyl, - C_{1-4} alkyl-C(O)O-(C_{1-4})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), amino(C₁₋₄)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-4})alkyl, (halo)₁₋₃(C_{1-4})alkoxy, hydroxy, hydroxy(C_{1-4})alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C_{1-4})alkyl, aryl(C_{1-4})alkyl, heteroaryl(C_{1-4})alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxy(C_{1-4})alkyl, carboxyl, carboxyl(C_{1-4})alkyl,

amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino (C_{1-4}) alkyl (wherein amino is

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substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-4})alkyl, (halo)₁₋₃(C_{1-4})alkoxy, hydroxy and hydroxy(C_{1-4})alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl, heterocyclyl, aryl, heteroaryl (wherein cycloalkyl, heterocyclyl, aryl and heteroaryl are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxy(C_{1-4})alkyl, carboxyl, carboxyl(C₁₋₄)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino(C_{1-4})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-4})alkyl, $(halo)_{1-3}(C_{1-4})alkoxy$, hydroxy and hydroxy $(C_{1-4})alkyl$; and, wherein heterocyclyl is optionally substituted with oxo), -(O-(CH₂)₁₋₆)₀₋₅-O-, $-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-O-, -O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-O -(O-(CH_2)_{1-6})_{0-5}-NR_{6-}$, $-O-(CH_2)_{1-6}-NR_{6-}(CH_2)_{1-6}-O-$, $-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-NR_{6-}$, $-(O-(CH_2)_{1-6})_{0-5}-S-$, $-O-(CH_2)_{1-6}-S-(CH_2)_{1-6}-O-$, $-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-S-$, $-NR_6-$, $-NR_6-NR_7-$, $-NR_6-(CH_2)_{1-6}-NR_7-$, $-NR_6-(CH_2)_{1-6}-NR_7-(CH_2)_{1-6}-NR_8-$, $-NR_6-C(O)-$, $-C(O)-NR_6-$, $-C(O)-(CH_2)_{0-6}-NR_6-(CH_2)_{0-6}-C(O) -NR_6-(CH_2)_{0-6}-C(O)-(CH_2)_{1-6}-C(O)-(CH_2)_{0-6}-NR_{7-}$, $-NR_6-C(O)-NR_{7-}$, $-NR_6-C(NR_7)-NR_8-$, $-O-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-S-$, $-S-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-O-$, $-S-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-S-$, $-NR_6-(CH_2)_{1-6}-S-(CH_2)_{1-6}-NR_7-$ and $-SO_2-$ (wherein R₆, R₇ and R₈ are independently selected from the group consisting of hydrogen, C_{1-4} alkyl, C_{1-4} alkoxy(C_{1-4})alkyl, carboxyl(C_{1-4})alkyl, amino(C₁₋₄)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), hydroxy(C_{1-4})alkyl, heterocyclyl(C_{1-4})alkyl, aryl(C_{1-4})alkyl and heteroaryl(C₁₋₄)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C₁₋₄alkyl, C₁₋₄alkoxy, C_{1-4} alkoxy(C_{1-4})alkyl, carboxyl, carboxyl(C_{1-4})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and

 C_{1-4} alkyl), amino (C_{1-4}) alkyl (wherein amino is substituted with a substituent

independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-4})alkyl, (halo)₁₋₃(C_{1-4})alkoxy, hydroxy and hydroxy(C_{1-4})alkyl; and, wherein heterocyclyl is optionally substituted with oxo));

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with the proviso that, if A and E are selected from a hydrogen substituted carbon atom, then R₂ is selected from the group consisting of $-C_{2-4}$ alkynyl-, $-O_{-}(C_{1-4})$ alkyl-O-, $-O_{-}(C_{2-4})$ alkenyl-O-, $-O_{-}(C_{2-4})$ alkynyl-O-, -C(O)-(C₁₋₄)alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are straight carbon chains optionally substituted with one to four substituents independently selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxy(C_{1-4})alkyl, carboxyl, carboxyl(C_{1-4})alkyl, -C(O)O-(C₁₋₄)alkyl, -C₁₋₄alkyl-C(O)O-(C₁₋₄)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino (C_{1-4}) alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), halogen, $(halo)_{1-3}(C_{1-4})$ alkyl, $(halo)_{1-3}(C_{1-4})$ alkoxy, hydroxy, hydroxy (C_{1-4}) alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C_{1-4})alkyl, aryl(C_{1-4})alkyl, heteroaryl(C_{1-4})alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C₁₋₄alkyl, C_{1-4} alkoxy, C_{1-4} alkoxy(C_{1-4})alkyl, carboxyl, carboxyl(C_{1-4})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino(C_{1-4})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-4})alkyl, (halo)₁₋₃(C_{1-4})alkoxy, hydroxy and hydroxy(C₁₋₄)alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl (wherein cycloalkyl is optionally substituted with one to four substituents independently selected from the group consisting of C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkoxy(C₁₋₄)alkyl, carboxyl, carboxyl(C_{1-4})alkyl, amino (substituted with a substituent independently

selected from the group consisting of hydrogen and C_{1-4} alkyl), amino(C_{1-4})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), halogen, (halo)₁₋₃(C₁₋₄)alkyl, $(halo)_{1-3}(C_{1-4})alkoxy$, hydroxy and hydroxy $(C_{1-4})alkyl$), $-(O-(CH_2)_{1-6})_{1-5}-O-$, 5 -O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-O-, -O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-O-, $-(O-(CH_2)_{1-6})_{1-5}-NR_{6-}$, $-O-(CH_2)_{1-6}-NR_{6-}(CH_2)_{1-6}-O-$, $-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-NR_{6-}$, $-(O-(CH_2)_{1-6})_{0-5}-S-$, $-O-(CH_2)_{1-6}-S-(CH_2)_{1-6}-O-$, -O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-S-, -NR₆-NR₇-, -NR₆-(CH₂)₁₋₆-NR₇-, -NR₆-(CH₂)₁₋₆-NR₇-(CH₂)₁₋₆-NR₈-, -NR₉-C(O)-, -C(O)-NR₉-, 10 $-C(O)-(CH_2)_{0-6}-NR_6-(CH_2)_{0-6}-C(O) -NR_6-(CH_2)_{0-6}-C(O)-(CH_2)_{1-6}-C(O)-(CH_2)_{0-6}-NR_7-$, $-NR_6-C(O)-NR_7-$, $-NR_6-C(NR_7)-NR_8-$, $-O-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-S-$, $-S-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-O-$, $-S-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-S-$ and $-NR_6-(CH_2)_{1-6}-S-(CH_2)_{1-6}-NR_7-$ (wherein R_6 , R₇ and R₈ are independently selected from the group consisting of hydrogen, 15 C_{1-4} alkyl, C_{1-4} alkyl, carboxyl(C_{1-4})alkyl, amino(C_{1-4})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), hydroxy(C₁₋₄)alkyl, heterocyclyl(C_{1-4})alkyl, aryl(C_{1-4})alkyl and heteroaryl(C_{1-4})alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally 20 substituted with one to four substituents independently selected from the group consisting of C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkoxy(C₁₋₄)alkyl, carboxyl, carboxyl(C₁₋₄)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino(C_{1-4})alkyl (wherein amino is substituted with a substituent independently selected from the 25 group consisting of hydrogen and C₁₋₄alkyl), halogen, (halo)₁₋₃(C₁₋₄)alkyl, $(halo)_{1-3}(C_{1-4})$ alkoxy, hydroxy and hydroxy (C_{1-4}) alkyl; and, wherein heterocyclyl is optionally substituted with oxo); and, wherein R₉ is selected from the group consisting of C₁₋₄alkyl, C₁₋₄alkoxy(C₁₋₄)alkyl, carboxyl(C_{1-4})alkyl, amino(C_{1-4})alkyl (wherein amino is substituted with a 30 substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), hydroxy(C_{1-4})alkyl, heterocyclyl(C_{1-4})alkyl, aryl(C_{1-4})alkyl and heteroaryl(C₁₋₄)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl

substituents are optionally substituted with one to four substituents

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independently selected from the group consisting of C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} alkoxy(C_{1-4})alkyl, carboxyl, carboxyl(C_{1-4})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino(C_{1-4})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-4})alkyl, (halo)₁₋₃(C_{1-4})alkoxy, hydroxy and hydroxy(C_{1-4})alkyl; and, wherein heterocyclyl is optionally substituted with oxo)).

6. The compound of claim 1 wherein R₂ is selected from the group consisting of

-C₁₋₈alkyl- (optionally substituted with one to three substituents independently selected from the group consisting of halogen, hydroxy and oxo); aryl, heteroaryl, -(O-(CH₂)₁₋₆)₀₋₅-O-, -O-(CH₂)₁₋₆-NR₆-(CH₂)₁₋₆-O-,

-O-(CH₂)₁₋₆-S-(CH₂)₁₋₆-O- and -NR₆- (wherein R₆, R₇ and R₈ are independently selected from the group consisting of hydrogen, C₁₋₄alkyl and

C₁₋₄alkoxy(C₁₋₄)alkyl);

with the proviso that, if A and E are selected from a hydrogen substituted carbon atom, then R_2 is selected from the group consisting of $-(O-(CH_2)_{1-6})_{1-5}-O-$, $-(O-(CH_2)_{1-6})_{1-5}-NR_6-$, $-O-(CH_2)_{1-6}-NR_6-$ (CH₂)₁₋₆-O- and $-NR_6-$ (CH₂)₁₋₆-NR₇ $-(CH_2)_{1-6}-NR_8-$ (wherein R_6 , R_7 and R_8 are independently selected from the group consisting of hydrogen, C_{1-4} alkyl and hydroxy(C_{1-4})alkyl).

The compound of claim 1 wherein R₂ is selected from the group consisting of -C₁₋₈alkyl- (optionally substituted with one to two substituents independently selected from the group consisting of halogen, hydroxy and oxo); phenyl,
 pyridinyl, -(O-(CH₂)₂)₁₋₄-O-, -O-(CH₂)₂-NR₆-(CH₂)₂-O-,
-O-(CH₂)₂-S-(CH₂)₂-O- and -NR₆- (wherein R₆, R₇ and R₈ are independently selected from the group consisting of hydrogen, C₁₋₃alkyl and C₁₋₂alkoxy(C₁₋₂)alkyl);

with the proviso that, if A and E are selected from a hydrogen substituted carbon atom, then R_2 is selected from the group consisting of $-(O-(CH_2)_2)_{1-4}-O-$, $-(O-(CH_2)_2)_{2}-NR_6-$, $-O-(CH_2)_{2}-NR_6-$ (CH₂)₂-O- and

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-NR₆-(CH₂)₂-NR₇-(CH₂)₂-NR₈- (wherein R₆, R₇ and R₈ are independently selected from the group consisting of hydrogen, C_{1-3} alkyl and hydroxy(C_{1-2})alkyl).

- The compound of claim 1 wherein R₁ and R₃ are independently selected from the group consisting of hydrogen, C₁₋₄alkyl, C₂₋₄alkenyl, C₂₋₄alkynyl (wherein alkyl, alkenyl and alkynyl are optionally substituted with a substituent selected from the group consisting of C_{1-4} alkoxy, alkoxy(C_{1-4})alkyl, carboxyl, carboxyl(C₁₋₄)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), amino(C₁₋₄)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), (halo)₁₋₃, (halo)₁₋₃(C_{1-4})alkyl, $(\text{halo})_{1-3}(C_{1-4})$ alkoxy, hydroxy, hydroxy (C_{1-4}) alkyl and oxo), C_{1-4} alkoxy, C_{1-4} alkoxycarbonyl, (halo)₁₋₃(C_{1-4})alkoxy, C_{1-4} alkylthio, aryl, heteroaryl (wherein aryl and heteroaryl are optionally substituted with a substituent selected from the group consisting of C₁₋₄alkyl, C₁₋₄alkoxy, alkoxy(C₁₋₄)alkyl, carboxyl, carboxyl(C₁₋₄)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), amino(C₁₋₄)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), halogen, $(halo)_{1-3}(C_{1-4})alkyl$, $(halo)_{1-3}(C_{1-4})alkoxy$, hydroxy and hydroxy $(C_{1-4})alkyl$), amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), cyano, halogen, hydroxy and nitro.
- 9. The compound of claim 1 wherein R₁ and R₃ are independently selected from the group consisting of hydrogen, C₁₋₄alkyl (optionally substituted with a substituent selected from the group consisting of C₁₋₄alkoxy, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), (halo)₁₋₃, hydroxy and oxo), C₁₋₄alkoxy, C₁₋₄alkoxycarbonyl, (halo)₁₋₃(C₁₋₄)alkoxy, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), halogen, hydroxy and nitro.

- 10. The compound of claim 1 wherein R_1 and R_3 are hydrogen.
- 11. The compound of claim 1 wherein a compound of Formula (I) is selected from a compound of Formula (Iaa):

$$R_1$$
 A
 R_2
 R_3
 R_4
 R_2

Formula (Iaa)

wherein

5 A and E are independently selected from the group consisting of a hydrogen substituted

carbon atom and a nitrogen atom; wherein N is independently selected from the group consisting of 1*H*-indole, 1*H*-pyrrolo[2,3-*b*]pyridine and 1*H*-indazole;

R₄ and R₅ are independently selected from C₁₋₈alkyl, C₂₋₈alkenyl and C₂₋₈alkynyl optionally substituted with oxo;

R₂ is selected from the group consisting of -C₁₋₈alkyl-, -C₂₋₈alkenyl-, -C₂₋₈alkynyl-,
-O-(C₁₋₈)alkyl-O-, -O-(C₂₋₈)alkenyl-O-, -O-(C₂₋₈)alkynyl-O-,
-C(O)-(C₁₋₈)alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl
linking groups are straight carbon chains optionally substituted with one to four substituents independently selected from the group consisting of C₁₋₈alkyl,
C₁₋₈alkoxy, C₁₋₈alkoxy(C₁₋₈)alkyl, carboxyl, carboxyl(C₁₋₈)alkyl,
-C(O)O-(C₁₋₈)alkyl, -C₁₋₈alkyl-C(O)O-(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and

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 C_{1-4} alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), halogen, $(\text{halo})_{1,3}(C_{1,8})$ alkyl, $(\text{halo})_{1,3}(C_{1,8})$ alkoxy, hydroxy, hydroxy $(C_{1,8})$ alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C₁₋₈)alkyl, $aryl(C_{1-8})alkyl$, heteroaryl $(C_{1-8})alkyl$, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C₁₋₈alkyl, C₁₋₈alkoxy, C₁₋₈alkoxy(C₁₋₈)alkyl, carboxyl, carboxyl(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino (C_{1-8}) alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), halogen, (halo)₁₋₃(C₁₋₈)alkyl, $(\text{halo})_{1-3}(C_{1-8})$ alkoxy, hydroxy and hydroxy (C_{1-8}) alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl, heterocyclyl, aryl, heteroaryl (wherein cycloalkyl, heterocyclyl, aryl and heteroaryl are optionally substituted with one to four substituents independently selected from the group consisting of C₁₋₈alkyl, C₁₋₈alkoxy, C₁₋₈alkoxy(C₁₋₈)alkyl, carboxyl, carboxyl(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), amino(C₁₋₈)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, (halo)₁₋₃(C₁₋₈)alkoxy, hydroxy and hydroxy(C₁₋₈)alkyl; and, wherein heterocyclyl is optionally substituted with oxo), -(O-(CH₂)₁₋₆)₀₋₅-O-, -O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-O-, $-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-O-$, $-(O-(CH_2)_{1-6})_{0-5}-NR_{6-}$, -O-(CH₂)₁₋₆-NR₆-(CH₂)₁₋₆-O-, -O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-NR₆-, -(O-(CH₂)₁₋₆)₀₋₅-S-, $-O-(CH_2)_{1-6}-S-(CH_2)_{1-6}-O-$, $-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-S-$, $-NR_6-$, $-NR_6-NR_7-$, -NR₆-(CH₂)₁₋₆-NR₇-, -NR₆-(CH₂)₁₋₆-NR₇-(CH₂)₁₋₆-NR₈-, -NR₆-C(O)-, -C(O)-NR₆-, $-C(O)-(CH_2)_{0-6}-NR_6-(CH_2)_{0-6}-C(O) -NR_6-(CH_2)_{0-6}-C(O)-(CH_2)_{1-6}-C(O)-(CH_2)_{0-6}-NR_{7-}$, $-NR_6-C(O)-NR_{7-}$ $-NR_6-C(NR_7)-NR_8-$, $-O-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-S-$, $-S-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-O-$, -S-(CH₂)₁₋₆-NR₆-(CH₂)₁₋₆-S-, -NR₆-(CH₂)₁₋₆-S-(CH₂)₁₋₆-NR₇- and -SO₂- (wherein

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 R_6 , R_7 and R_8 are independently selected from the group consisting of hydrogen, C_{1-8} alkyl, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl(C_{1-8})alkyl, amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), hydroxy(C_{1-8})alkyl, heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl and heteroaryl(C_{1-8})alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, (halo)₁₋₃(C_{1-8})alkoxy, hydroxy and hydroxy(C_{1-8})alkyl; and, wherein heterocyclyl is optionally substituted with oxo));

with the proviso that, if A and E are selected from a hydrogen substituted carbon atom, then R₂ is selected from the group consisting of -C₂₋₈alkynyl-, -O-(C₁₋₈)alkyl-O-, $-O-(C_{2-8})$ alkenyl-O-, $-O-(C_{2-8})$ alkynyl-O-, $-C(O)-(C_{1-8})$ alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are straight carbon chains optionally substituted with one to four substituents independently selected from the group consisting of C₁₋₈alkyl, C₁₋₈alkoxy, C₁₋₈alkoxy(C₁₋₈)alkyl, carboxyl, carboxyl(C₁₋₈)alkyl, -C(O)O-(C₁₋₈)alkyl, -C₁₋₈alkyl-C(O)O-(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), amino(C₁₋₈)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, (halo)₁₋₃(C_{1-8})alkoxy, hydroxy, hydroxy(C_{1-8})alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl. heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl, heteroaryl(C_{1-8})alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents

independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and

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 C_{1-4} alkyl), amino (C_{1-8}) alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), halogen, $(\text{halo})_{1-3}(C_{1-8})$ alkyl, $(\text{halo})_{1-3}(C_{1-8})$ alkoxy, hydroxy and hydroxy (C_{1-8}) alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl (wherein cycloalkyl is optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), amino(C₁₋₈)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, (halo)₁₋₃(C_{1-8})alkoxy, hydroxy and hydroxy(C_{1-8})alkyl), -(O-(CH_2)₁₋₆)₁₋₅-O-, -O-(CH_2)₁₋₆-O-(CH_2)₁₋₆-O-, $-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-O-$, $-(O-(CH_2)_{1-6})_{1-5}-NR_{6-}$, -O-(CH₂)₁₋₆-NR₆-(CH₂)₁₋₆-O-, -O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-NR₆-, -(O-(CH₂)₁₋₆)₀₋₅-S-, -O-(CH₂)₁₋₆-S-(CH₂)₁₋₆-O-, -O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-S-, -NR₆-NR₇-, $-NR_{6}-(CH_{2})_{1-6}-NR_{7}-$, $-NR_{6}-(CH_{2})_{1-6}-NR_{7}-$, $-NR_{9}-(CH_{2})_{1-6}-NR_{8}-$, $-NR_{9}-(CO)-$, $-C(O)-NR_{9}-$, $-C(O)-(CH_2)_{0-6}-NR_6-(CH_2)_{0-6}-C(O) -NR_{6}-(CH_{2})_{0-6}-C(O)-(CH_{2})_{1-6}-C(O)-(CH_{2})_{0-6}-NR_{7}-$, $-NR_{6}-C(O)-NR_{7}-$, $-NR_6-C(NR_7)-NR_8-$, $-O-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-S-$, $-S-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-O-$, $-S-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-S-$ and $-NR_6-(CH_2)_{1-6}-S-(CH_2)_{1-6}-NR_7-$ (wherein R_6 , R_7 and R_8 are independently selected from the group consisting of hydrogen, $C_{1.8}$ alkyl, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl(C_{1-8})alkyl, amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and $C_{1.4}$ alkyl), hydroxy($C_{1.8}$)alkyl, heterocyclyl($C_{1.8}$)alkyl, aryl($C_{1.8}$)alkyl and heteroaryl(C₁₋₈)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), amino(C₁₋₈)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, $(halo)_{1-3}(C_{1-8})$ alkoxy, hydroxy and hydroxy (C_{1-8}) alkyl; and, wherein heterocyclyl is optionally substituted with oxo); and, wherein R₉ is selected from the group

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consisting of C_{1-8} alkyl, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl(C_{1-8})alkyl, amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), hydroxy(C_{1-8})alkyl, heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl and heteroaryl(C_{1-8})alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo) $_{1-3}$ (C_{1-8})alkyl, (halo) $_{1-3}$ (C_{1-8})alkoxy, hydroxy and hydroxy(C_{1-8})alkyl; and, wherein heterocyclyl is optionally substituted with oxo)); and,

15 R₁ and R₃ are independently selected from the group consisting of hydrogen, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl (wherein alkyl, alkenyl and alkynyl are optionally substituted with a substituent selected from the group consisting of C₁₋₈alkoxy, alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and 20 C_{1-4} alkyl), amino (C_{1-8}) alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), $(halo)_{1-3}, (halo)_{1-3}(C_{1-8})alkyl, (halo)_{1-3}(C_{1-8})alkoxy, hydroxy, hydroxy(C_{1-8})alkyl$ and oxo), C₁₋₈alkoxy, C₁₋₈alkoxycarbonyl, (halo)₁₋₃(C₁₋₈)alkoxy, C₁₋₈alkylthio, aryl, heteroaryl (wherein aryl and heteroaryl are optionally substituted with a substituent 25 selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino (C_{1-8}) alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, 30 $(halo)_{1-3}(C_{1-8})$ alkoxy, hydroxy and hydroxy (C_{1-8}) alkyl), amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), cyano, halogen, hydroxy and nitro:

and pharmaceutically acceptable salts thereof.

12. The compound of claim 1 wherein a compound of Formula (I) is selected from the group consisting of:

R₁

$$R_4$$
 R_2
 R_5
 R_4
 R_5
 R_4
 R_5
 R_4
 R_5
 R_4
 R_5
 R_4
 R_5
 R_5
 R_4
 R_5
 R_5
 R_6
 R_7
 R_8
 R_8
 R_9
 R_9

5 wherein

 R_4 and R_5 are independently selected from C_{1-8} alkyl, C_{2-8} alkenyl and C_{2-8} alkynyl optionally substituted with oxo;

 R_2 is selected from the group consisting of $-C_{1-8}$ alkyl-, $-C_{2-8}$ alkenyl-, $-C_{2-8}$ alkynyl-, $-O-(C_{1-8})$ alkyl-O-, $-O-(C_{2-8})$ alkynyl-O-, $-O-(C_{2-8})$ alkynyl-O-,

 $-C(O)-(C_{1-8})$ alkyl-C(O)- (wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are straight carbon chains optionally substituted with one to four substituents independently selected from the group consisting of C₁₋₈alkyl, C_{1-8} alkoxy, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, 5 -C(O)O-(C_{1-8})alkyl, - C_{1-8} alkyl-C(O)O-(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino (C_{1-8}) alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), halogen, $(halo)_{1-3}(C_{1-8})$ alkyl, $(halo)_{1-3}(C_{1-8})$ alkoxy, hydroxy, hydroxy (C_{1-8}) alkyl and 10 oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl, heterocyclyl(C₁₋₈)alkyl, aryl(C_{1-8})alkyl, heteroaryl(C_{1-8})alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl 15 substituents are optionally substituted with one to four substituents independently selected from the group consisting of C₁₋₈alkyl, C₁₋₈alkoxy, C₁₋₈alkoxy(C₁₋₈)alkyl, carboxyl, carboxyl(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), amino(C₁₋₈)alkyl (wherein amino is substituted with a substituent independently selected from the 20 group consisting of hydrogen and C₁₋₄alkyl), halogen, (halo)₁₋₃(C₁₋₈)alkyl. (halo)₁₋₃(C₁₋₈)alkoxy, hydroxy and hydroxy(C₁₋₈)alkyl; and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl, heterocyclyl, aryl, heteroaryl (wherein cycloalkyl, heterocyclyl, aryl and heteroaryl are optionally substituted with one to four substituents independently selected from the group consisting of C₁₋₈alkyl, C₁₋₈alkoxy, C₁₋₈alkoxy(C₁₋₈)alkyl, 25 carboxyl, carboxyl(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C1-4alkyl), amino(C1-8)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), halogen, (halo)₁₋₃(C₁₋₈)alkyl, 30 $(halo)_{1-3}(C_{1-8})$ alkoxy, hydroxy and hydroxy (C_{1-8}) alkyl; and, wherein heterocyclyl is optionally substituted with oxo), -(O-(CH₂)₁₋₆)₀₋₅-O-, -O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-O-, $-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-O-$, $-(O-(CH_2)_{1-6})_{0-5}-NR_{6-}$,

-O-(CH₂)₁₋₆-NR₆-(CH₂)₁₋₆-O-, -O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-NR₆-, -(O-(CH₂)₁₋₆)₀₋₅-S-,

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-O-(CH₂)₁₋₆-S-(CH₂)₁₋₆-O-, -O-(CH₂)₁₋₆-O-(CH₂)₁₋₆-S-, -NR₆-, -NR₆-NR₇-,
-NR₆-(CH₂)₁₋₆-NR₇-, -NR₆-(CH₂)₁₋₆-NR₇-(CH₂)₁₋₆-NR₈-, -NR₆-C(O)-, -C(O)-NR₆-,
-C(O)-(CH₂)₀₋₆-NR₆-(CH₂)₀₋₆-C(O)-,
-NR₆-(CH₂)₀₋₆-C(O)-(CH₂)₁₋₆-C(O)-(CH₂)₀₋₆-NR₇-, -NR₆-C(O)-NR₇-,
-NR₆-C(NR₇)-NR₈-, -O-(CH₂)₁₋₆-NR₆-(CH₂)₁₋₆-S-, -S-(CH₂)₁₋₆-NR₆-(CH₂)₁₋₆-O-,
-S-(CH₂)₁₋₆-NR₆-(CH₂)₁₋₆-S-, -NR₆-(CH₂)₁₋₆-S-(CH₂)₁₋₆-NR₇- and -SO₂- (wherein R₆, R₇ and R₈ are independently selected from the group consisting of hydrogen,
C₁₋₈alkyl, C₁₋₈alkoxy(C₁₋₈)alkyl, carboxyl(C₁₋₈)alkyl, amino(C₁₋₈)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), hydroxy(C₁₋₈)alkyl, heterocyclyl(C₁₋₈)alkyl,

aryl(C₁₋₈)alkyl and heteroaryl(C₁₋₈)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C₁₋₈alkyl, C₁₋₈alkoxy, C₁₋₈alkoxy(C₁₋₈)alkyl, carboxyl, carboxyl(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), amino(C₁₋₈)alkyl (wherein amino is substituted with a substituent

independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, (halo)₁₋₃(C_{1-8})alkoxy, hydroxy and hydroxy(C_{1-8})alkyl; and, wherein heterocyclyl is optionally substituted with oxo));

with the proviso that, if A and E are selected from a hydrogen substituted carbon atom,

then R₂ is selected from the group consisting of -C₂₋₈alkynyl-, -O-(C₁₋₈)alkyl-O-,
-O-(C₂₋₈)alkenyl-O-, -O-(C₂₋₈)alkynyl-O-, -C(O)-(C₁₋₈)alkyl-C(O)- (wherein any of
the foregoing alkyl, alkenyl and alkynyl linking groups are straight carbon chains
optionally substituted with one to four substituents independently selected from the
group consisting of C₁₋₈alkyl, C₁₋₈alkoxy, C₁₋₈alkoxy(C₁₋₈)alkyl, carboxyl,
carboxyl(C₁₋₈)alkyl, -C(O)O-(C₁₋₈)alkyl, -C₁₋₈alkyl-C(O)O-(C₁₋₈)alkyl, amino
(substituted with a substituent independently selected from the group consisting of
hydrogen and C₁₋₄alkyl), amino(C₁₋₈)alkyl (wherein amino is substituted with a
substituent independently selected from the group consisting of hydrogen and

 C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, (halo)₁₋₃(C_{1-8})alkoxy, hydroxy, hydroxy(C_{1-8})alkyl and oxo; and, wherein any of the foregoing alkyl, alkenyl and alkynyl linking groups are optionally substituted with one to two substituents independently selected from the group consisting of heterocyclyl, aryl, heteroaryl,

heterocyclyl(C_{1-8})alkyl, aryl(C_{1-8})alkyl, heteroaryl(C_{1-8})alkyl, spirocycloalkyl and spiroheterocyclyl (wherein any of the foregoing cycloalkyl, heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy,

- C₁₋₈alkoxy(C₁₋₈)alkyl, carboxyl, carboxyl(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), amino(C₁₋₈)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), halogen, (halo)₁₋₃(C₁₋₈)alkyl, (halo)₁₋₃(C₁₋₈)alkoxy, hydroxy and hydroxy(C₁₋₈)alkyl; and wherein any of the foregoing beterocyclyl substituents are optionally
- and, wherein any of the foregoing heterocyclyl substituents are optionally substituted with oxo)), cycloalkyl (wherein cycloalkyl is optionally substituted with one to four substituents independently selected from the group consisting of C₁₋₈alkyl, C₁₋₈alkoxy, C₁₋₈alkoxy(C₁₋₈)alkyl, carboxyl, carboxyl(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of
- hydrogen and C_{1-4} alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, (halo)₁₋₃(C_{1-8})alkoxy, hydroxy and hydroxy(C_{1-8})alkyl), -(O-(CH_2)₁₋₆)₁₋₅-O-, -O-(CH_2)₁₋₆-O-(CH_2)₁₋₆-O-,
 - $-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-O-$, $-(O-(CH_2)_{1-6})_{1-5}-NR_{6}-$,
- 20 $-O-(CH_2)_{1-6}-NR_6-(CH_2)_{1-6}-O-, -O-(CH_2)_{1-6}-O-(CH_2)_{1-6}-NR_6-, -(O-(CH_2)_{1-6})_{0-5}-S-,$
 - $\hbox{-O-}(CH_2)_{1\text{-}6}\hbox{-S-}(CH_2)_{1\text{-}6}\hbox{-O-}, \hbox{-O-}(CH_2)_{1\text{-}6}\hbox{-O-}(CH_2)_{1\text{-}6}\hbox{-S-}, \hbox{-NR}_6\hbox{-NR}_{7}\hbox{-},$
 - $-NR_{6}-(CH_{2})_{1-6}-NR_{7}-,\ -NR_{6}-(CH_{2})_{1-6}-NR_{7}-(CH_{2})_{1-6}-NR_{8}-,\ -NR_{9}-C(O)-,\ -C(O)-NR_{9}-,\ -NR_{9}-(CH_{2})_{1-6}-NR_{9}-,\ -NR_{9}-C(O)-,\ -C(O)-NR_{9}-,\ -NR_{9}-(CH_{2})_{1-6}-NR_{9}-,\ -NR_{9}-(CH_{2})_{1-6}-NR_{9}-,\ -NR_{9}-C(O)-,\ -C(O)-NR_{9}-,\ -NR_{9}-(CH_{2})_{1-6}-NR_{9}-,\ -NR_{9}-C(O)-,\ -C(O)-NR_{9}-,\ -NR_{9}-(CH_{2})_{1-6}-NR_{9}-,\ -NR_{9}-(CH_{$
 - $-C(O)-(CH_2)_{0-6}-NR_6-(CH_2)_{0-6}-C(O)-,$
 - $-NR_6-(CH_2)_{0-6}-C(O)-(CH_2)_{1-6}-C(O)-(CH_2)_{0-6}-NR_{7}-$, $-NR_6-C(O)-NR_{7}-$,
- 25 -NR₆-C(NR₇)-NR₈-, -O-(CH₂)₁₋₆-NR₆-(CH₂)₁₋₆-S-, -S-(CH₂)₁₋₆-NR₆-(CH₂)₁₋₆-O-,
- -S-(CH₂)₁₋₆-NR₆-(CH₂)₁₋₆-S- and -NR₆-(CH₂)₁₋₆-S-(CH₂)₁₋₆-NR₇- (wherein R₆, R₇ and R₈ are independently selected from the group consisting of hydrogen, C₁₋₈alkyl,
 - C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl(C_{1-8})alkyl, amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of
- hydrogen and C₁₋₄alkyl), hydroxy(C₁₋₈)alkyl, heterocyclyl(C₁₋₈)alkyl, aryl(C₁₋₈)alkyl and heteroaryl(C₁₋₈)alkyl (wherein the foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C₁₋₈alkyl, C₁₋₈alkoxy, C₁₋₈alkoxy(C₁₋₈)alkyl,

carboxyl, carboxyl(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), amino(C₁₋₈)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), halogen, (halo)₁₋₃(C₁₋₈)alkyl, (halo)₁₋₃(C₁₋₈)alkoxy, hydroxy and hydroxy(C₁₋₈)alkyl; and, wherein heterocyclyl is optionally substituted with oxo); and, wherein R₉ is selected from the group consisting of C₁₋₈alkyl, C₁₋₈alkoxy(C₁₋₈)alkyl, carboxyl(C₁₋₈)alkyl, amino(C₁₋₈)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), hydroxy(C₁₋₈)alkyl, heterocyclyl (C₁₋₈)alkyl, aryl(C₁₋₈)alkyl and heteroaryl(C₁₋₈)alkyl (wherein the foregoing heterocyclyl aryl and heteroaryl substituents are ontionally substituted

foregoing heterocyclyl, aryl and heteroaryl substituents are optionally substituted with one to four substituents independently selected from the group consisting of C_{1-8} alkyl, C_{1-8} alkoxy, C_{1-8} alkoxy(C_{1-8})alkyl, carboxyl, carboxyl(C_{1-8})alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), amino(C_{1-8})alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, (halo)₁₋₃(C_{1-8})alkoxy, hydroxy and hydroxy(C_{1-8})alkyl; and, wherein heterocyclyl is optionally substituted with oxo)); and,

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R₁ and R₃ are independently selected from the group consisting of hydrogen, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl (wherein alkyl, alkenyl and alkynyl are optionally substituted with a substituent selected from the group consisting of C₁₋₈alkoxy, alkoxy(C₁₋₈)alkyl, carboxyl, carboxyl(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), amino(C₁₋₈)alkyl (wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), (halo)₁₋₃, (halo)₁₋₃(C₁₋₈)alkyl, (halo)₁₋₃(C₁₋₈)alkoxy, hydroxy(C₁₋₈)alkyl and oxo), C₁₋₈alkoxy, C₁₋₈alkoxycarbonyl, (halo)₁₋₃(C₁₋₈)alkoxy, C₁₋₈alkylthio, aryl, heteroaryl (wherein aryl and heteroaryl are optionally substituted with a substituent selected from the group consisting of C₁₋₈alkyl, C₁₋₈alkoxy, alkoxy(C₁₋₈)alkyl, carboxyl, carboxyl(C₁₋₈)alkyl, amino (substituted with a substituent independently selected from the group consisting of hydrogen and C₁₋₄alkyl), amino(C₁₋₈)alkyl

(wherein amino is substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), halogen, (halo)₁₋₃(C_{1-8})alkyl, (halo)₁₋₃(C_{1-8})alkoxy, hydroxy and hydroxy(C_{1-8})alkyl), amino (substituted with a substituent independently selected from the group consisting of hydrogen and C_{1-4} alkyl), cyano, halogen, hydroxy and nitro;

and pharmaceutically acceptable salts thereof.

13. A compound of Formula (Ia1):

Formula (Ia1)

wherein R₄, R₂ and R₅ are dependently selected from:

R ₄	$\mathbf{R_2}$	R_5
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -O-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -O-(CH ₂) ₂ -O-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -O-(CH ₂) ₂ -O-(CH ₂) ₂ -O-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -N(Et)-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -N(Me)-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -N(<i>i</i> -Pr)-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
-(CH ₂) ₂ -	$-N(Me)-(CH_2)_2-N(Me)-(CH_2)_2-N(Me)-$	-(CH ₂) ₂ -;
-(CH ₂) ₂ -	-O-(CH2)2-N(2-hydroxy-Et)-(CH2)2-O-	-(CH ₂) ₂ -;
and,		
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -O-(CH ₂) ₂ -N(Me)-	-(CH ₂) ₃

14. A compound of Formula (Ib1):

Formula (Ib1)

wherein R_4 , R_2 and R_5 are dependently selected from:

$\mathbf{R_4}$	R_2	R ₅
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -O-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -O-(CH ₂) ₂ -O-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -O-(CH ₂) ₂ -O-(CH ₂) ₂ -O-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -N(Et)-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -S-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
-(CH ₂) ₅ -	-NH-	-(CH ₂) ₅ -;
-(CH ₂) ₅ -	-N(Et)-	-(CH ₂) ₅ -;
-(CH ₂) ₅ -	-NH-	-(CH ₂) ₄ -;
-(CH ₂) ₅ -	-N(Et)-	-(CH ₂) ₄ -;
-(CH ₂) ₄ -	-2,6-pyridinyl-	-(CH ₂) ₄ -;
-(CH ₂) ₄ -	-C(O)-(CH ₂) ₂ -	-(CH ₂) ₄ -;
-(CH ₂) ₄ -	-C(O)-	-(CH ₂) ₄ -;
-CH ₂ -	-CH[R](OH)-(CH ₂) ₆ -CH[R](OH)-	-CH ₂ -;
and,		
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -O-	-(CH ₂) ₂

15. A compound of Formula (If1):

Formula (If1)

wherein R₄, R₂ and R₅ are dependently selected from:

\mathbb{R}_4	R ₂	R ₅
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -N(Me)-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -N(Et)-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
and,		
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -N(2-OMe-Et)-(CH ₂) ₂ -O-	-(CH ₂) ₂

16. A compound of Formula (Ii1):

$$\begin{array}{c|c}
 & H & O \\
 & N & O \\
 & N & N \\
 & N & N \\
 & R_4 & R_5
\end{array}$$

Formula (Ii1)

wherein R_4 , R_2 and R_5 are dependently selected from:

R_2	R ₅
-1,3-phenyl-	-CH ₂ -;
-2,6-pyridinyl-	-CH ₂
	-1,3-phenyl-

17. A compound of Formula (Ij1):

 $\begin{array}{c}
 & H \\
 & O \\
 & N \\
 & R_5
\end{array}$

Formula (Ij1)

wherein R_4 , R_2 and R_5 are dependently selected from:

\mathbf{R}_4	R_2	\mathbf{R}_{5}

$-(CH_2)_2-$	-O-(CH ₂) ₂ -O-	-(CH ₂) ₂ -;
and,		
-(CH ₂) ₂ -	-O-(CH ₂) ₂ -O-(CH ₂) ₂ -O-	$-(CH_2)_2$

- 18. A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier.
- 5 19. A pharmaceutical composition made by mixing a compound of claim 1 and a pharmaceutically acceptable carrier.
 - 20. A method for preparing a pharmaceutical composition comprising mixing a compound of claim 1 and a pharmaceutically acceptable carrier.
 - 21. A method for treating or ameliorating a kinase mediated disorder comprising administering to a subject in need thereof a therapeutically effective amount of a compound of claim 1.
- 15 22. The method of claim 21 wherein the disorder is mediated by selective inhibition of a kinase selected from the group consisting of protein kinase C and glycogen synthase kinase-3.
- The method of claim 22 wherein the kinase is selected from the group
 consisting of protein kinase C α, protein kinase C β-II, protein kinase C γ and glycogen synthase kinase-3β.
- The method of claim 21 wherein the disorder is mediated by dual inhibition of at least two kinases selected from the group consisting of protein kinase C and
 glycogen synthase kinase-3.
 - 25. The method of claim 24 wherein at least two kinases are selected from the group consisting of protein kinase C α , protein kinase C β -II, protein kinase C γ and glycogen synthase kinase-3 β .

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- 26. The method of claim 21 wherein the therapeutically effective amount of the compound of claim 1 is from about 0.001 mg/kg/day to about 300 mg/kg/day.
- 27. The method of claim 21 wherein the kinase mediated disorder is selected from the group consisting of cardiovascular diseases, diabetes, diabetes-associated disorders, inflammatory diseases, immunological disorders, dermatological disorders, oncological disorders and CNS disorders.
- The method of claim 27 wherein cardiovascular diseases are selected from the group consisting of acute stroke, heart failure, cardiovascular ischemia, thrombosis, atherosclerosis, hypertension, restenosis, retinopathy of prematurity and age-related macular degeneration.
- The method of claim 27 wherein diabetes is selected from the group consisting
 of insulin dependent diabetes and Type II non-insulin dependent diabetes
 mellitus.
 - 30. The method of claim 27 wherein diabetes-associated disorders are selected from the group consisting of impaired glucose tolerance, diabetic retinopathy, proliferative retinopathy, retinal vein occlusion, macular edema, cardiomyopathy, nephropathy and neuropathy.
 - 31. The method of claim 27 wherein inflammatory diseases are selected from the group consisting of vascular permeability, inflammation, asthma, rheumatoid arthritis and osteoarthritis.
 - 32. The method of claim 27 wherein immunological disorders are selected from the group consisting of transplant tissue rejection, HIV-1 and PKC modulated immunological disorders.
 - 33. The method of claim 27 wherein dermatological disorders are selected from the group consisting of psoriasis, hair loss and baldness.

- 34. The method of claim 27 wherein oncological disorders are selected from the group consisting of cancer, tumor growth, uncontrolled cell proliferation, proliferative angiopathy and angiogenesis.
- 5 35. The method of claim 27 wherein central nervous system disorders are selected from the group consisting of chronic pain, neuropathic pain, epilepsy, chronic neurodegenerative conditions, dementia, Alzheimer's disease, mood disorders, schizophrenia, manic depression and neurotraumatic, cognitive decline and ischemia-related diseases.

- 36. The method of claim 21 further comprising a method for use for a compound of claim 1 as an adjunct to chemotherapy and radiation therapy.
- The method of claim 21 further comprising administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 18.
 - 38. The method of claim 37 wherein the therapeutically effective amount of a pharmaceutical composition of claim 18 is from about 0.001 mg/kg/day to about 300 mg/kg/day.
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- 39. The method of claim 35 wherein ischemia-related diseases are those resulting from head trauma or transient ischemic stroke.

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